

Neuromagnetic responses during unilateral periodic finger tapping to phasic contralateral finger tap stimulation

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1 Introduction

Humans can perform rhythmic voluntary movement without a benefit of an external cue such as a metronome beep sound. This suggests that there exists an “internal clock” in the nervous system generating the periodic rhythm [1]. In this paper, we investigate how rhythms of the internal clock are controlled or modulated. We assume that the periodic dynamics of the internal clock for the periodic finger tapping control can be modeled by a limit cycle oscillator. In general, single impulsive perturbations delivered to a limit cycle oscillator shift the phase of subsequent compared to the non-perturbed control case. The amount of phase shift, referred to as *phase reset* [2], as well as the transient behavior of the system, includes much information about the underlying dynamical system. For this reason, the phase resetting curves (PRCs) representing the phase reset as a function of the perturbation timing has been applied to understanding generation and control mechanisms of rhythmic activities of biological oscillators, e.g., circadian rhythm [2], neuronal firings [3], and EEG alpha rhythm [4]. In the field of motor control, it has been shown that periodic wrist movement exhibits phase reset in response to magnetic stimulation applied to the motor cortex [5].

Yamanishi et al. [6] have shown PRCs of the periodic finger tapping in response to a brief visual cue followed by a contra-lateral single finger tap, and discussed bimanual coordination based on the topological property of the PRCs. We continued their study, and tried to obtain PRC of the brain activity during the periodic finger tapping. To this end, we perturbed the neural activity during the tapping and thus the periodic right-index finger tapping movement by the single left-index finger tap, and responses of each to the perturbations were measured simultaneously. The neural responses were measured using magnetoencephalography (MEG) [7][8].

2 Methods

Eight right-handed normal male subjects participated in this study. The subjects started right-index finger tapping in time with a series of 30 auditory pulses (500 Hz tone) separated by fixed interval $N=600$ ms (paced mode). Following the end of the auditory pulse train, they were required to continue tapping at the established fixed rate (non-paced mode). During the non-paced mode, they were instructed to execute single left-index finger tap (contra-lateral to the periodic tapping) as rapid as possible in response to an auditory impulsive signal (2000 Hz tone) which was given randomly to the subjects at various phase within the tapping cycle. This left-index finger tap was considered as the perturbation to the internal clock controlling the periodic right-index finger tapping. Every ground-contact (tap) of the right-index finger was taken as the reference event. The phase ϕ of the right-index finger tapping cycle was defined as follows: (1) $\phi=0$ when a reference event occurs. (2) Phase of the state $t>0$ after the reference event in the tapping cycle is $\phi = t/N \pmod{1}$, where N is the period of the finger tapping. The phase of the right tapping cycle at the left-index finger tap is referred to as the stimulus phase ϕ_{stim} . Prior to these experiments, the subjects performed the control task in which no auditory impulsive signal for left-index finger tap was applied during the non-paced mode.

Neuromagnetic field (MEG) during the periodic tapping and in response to the perturbations were recorded using 122-channel SQUID planar gradiometer system (Neuromag 122). Every ground-contact (tap) of the right and left-index fingers was recorded using photoelectrical sensor. MEG waveform during the periodic right-index finger tapping in the control tasks, an epoch of either 4 s (2 s pre and 2 s post-reference event) was extracted and about 150 responses were averaged. For the analysis of the phase resetting of the neural activities, MEG data in response to stimulations were divided into 10 sets according to ϕ_{stim} .

Set k consists of data for $\phi_{\text{stim}} \in [0.1(k-1), 0.1k]$. Each set includes about 60 stimulations, and they were summed up from 2.4 s before to 2.4 s after the trigger reference event and divided by the number of the data for each set (averaged sum). The trigger reference event in the phase reset experiment was defined by the right-index finger tap *just before the left-index finger tap*. The averaged waveforms enable us to obtain PRCs of the MEG in the left sensorimotor cortex by plotting the color-coded magnitude of the averaged MEG responses against ϕ_{stim} . PRCs of the right-index finger tapping were obtained by plotting the timing of the right-finger tap against ϕ_{stim} .

3 Results

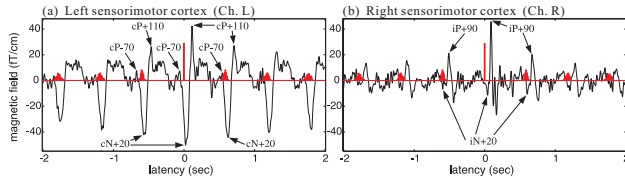


Figure 1: Neuromagnetic field (MEG) recorded from a channel located near (a) left and (b) right sensorimotor cortices during the periodic right-index finger tapping with the interval 600 ms (control task). Each abscissa is the latency ranged between -2 s to $+2$ s with respect to the right-index finger tap (ground-contact). Upward (red) histograms in each trace represent distribution of the timing of ground-contacts of right-index finger.

The averaged sum of MEG waveform recorded from channels located near the left (Ch. L) and right (Ch. R) sensorimotor cortices during the periodic right-index finger tapping (control task) is shown in Fig. 1. Comparing with the right-finger ground-contact timings, it showed periodic oscillation with the same period as the finger tapping. A positive peak at about 70 ms before, a negative peak at about 20 ms after, and a positive peak at about 110 ms after the trigger reference event were observed in channel L. These peaks are referred to as cP-70, cN+20, and cP+110, respectively, in this sequel. A negative peak at about 20 ms after and a positive peak at about 90 ms after the trigger reference event were observed in channel R. These peaks are referred to as iN+20 and iP+90, respectively, in this sequel. Our main interest was to clarify how these periodic MEG waveforms are perturbed by the phasic left-index finger tap stimulation.

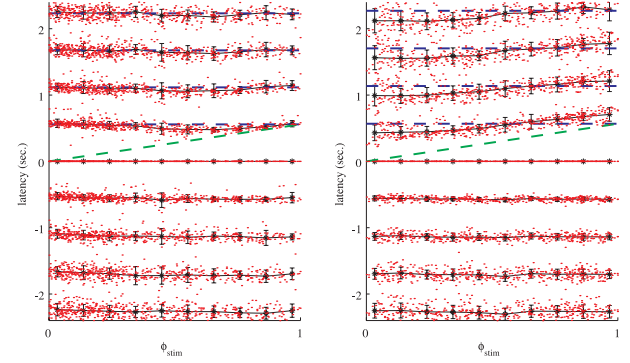


Figure 2: Phase resetting curves (PRCs) of right-index finger tapping. Left: Type 1 reset subject. Right: Type 0 reset subject. The abscissa is stimulation phase ϕ_{stim} . The ordinate is latency with respect to right-index finger tap (ground-contact) just prior to left-index finger tap stimulation. The left-index finger tap was applied along the (green) dashed diagonal line. Occurrences of right-index finger taps were plotted by (red) points and their mean latency within each set was indicated by asterisks with an SD bar. The (blue) dashed horizontal lines represent occurrences of right-index finger taps in the control case.

Figure 2 shows the PRCs for the right-index finger tapping. In Fig. 2 left, the average slope of every curve after the stimulation is zero, thus Type 1 reset in Winfree's definition [2]. In Fig. 2 right, the average slope of every curve after the stimulation is the period of the finger tapping rhythm, thus Type 0 reset [2]. Four out of eight subjects showed Type 1 phase reset, and other four subjects showed Type 0 phase reset. For general limit cycle oscillators, Type 0 phase reset is obtained for relatively strong perturbation, and Type 1 for weak one. The shapes of PRCs for the left sensorimotor cortex activities (Ch. L) (figures not shown) were similar to those of the finger tapping rhythm in each subject.

Figure 3 shows representative averaged MEG waveforms recorded from channel L and channel R for one Type 1 and one Type 0 subjects. In the both subjects, the temporal relationship between the right-finger taps and the two peaks cP-70 and cN+20 in the MEG waveform of channels L was extremely similar to the control until the appearance of the brain activity associated to the left-index finger tap stimulation. This similarity could also be observed about two taps after the stimulation, implying that the finger tapping rhythm and the brain activity returned to the original periodic oscillations.

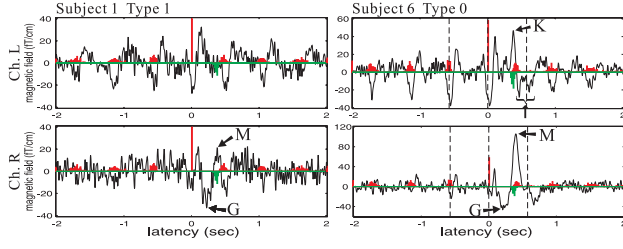


Figure 3: Representative averaged MEG waveforms of the channels located in the left and right sensorimotor cortices area (denoted by Ch.L and Ch. R respectively) in the subjects with Type 1 reset in the left and Type 0 reset in the right (phase resetting experiment, set 7). The upward (red) and downward (green) histograms represent the timing of the right and left-index finger ground-contacts, respectively.

During the transient, i.e., from the stimulation to about two taps after it, the MEG waveforms of Type 0 subjects were different from those of Type 1 subjects. Let us concentrate on the waveforms for set 7 (Fig. 3) to illustrate the phase reset of MEG and the difference between Type 1 and Type 0. The difference is summarized as follows: **(i)** In all Type 0 subjects, about 13 ± 17 ms after the left-index finger tap, the large positive peak corresponding to iN+20 for the left-index finger tap was detected in the channel L. We denote this peak as K. The peak K was either absent in two out of four Type 1 subjects, or relatively smaller, when it exists, than those in Type 0 subjects. **(ii)** The maximum value of the peak K, if it exists, was attained at least 80 ms after the small negative peak in the channel R (indicated by G in Fig. 3) corresponding to cP-70 for the left-finger tap. **(iii)** The peak K in the channel L, if it exists, also culminated earlier than the large positive peak in the channel R (indicated by M in Fig. 3) corresponding to cN+20 for the left-finger tap for four out of six Type 1 and Type 0 subjects. **(iv)** For every subject, the peak K preceded the first right-index finger tap after the left-index finger tap stimulation. In the Type 0 subject in Fig. 3, for example, this right-index finger tap was advanced (phase reset) about 130 ms compared to the control non-perturbed case. **(v)** The recovery of the MEG waveform in the channel L from the negative cN+20 for the first right-index finger tap after the stimulation to positive side in Type 0 subjects was slower than that in Type 1 subjects, and it formed relatively wide W-shaped valley indicated by the parenthesis in Fig. 3 upper-right.

4 Discussion

We first discuss the peaks in the MEG waveforms obtained from the channels on the left and right

sensorimotor cortices during the fast periodic right-index finger tapping (control non-perturbed case). Gerloff et al. [7] studied the left sensorimotor cortical physiology of the fast (2 Hz) repetitive right-thumb finger abduction, and clarified the existence and its interpretation of two dominant components. Comparing with their results, cP-70 and cN+20 obtained in our experiment (Fig. 1(a)) may be interpreted as MF which is related to the generation of corticospinal volleys in the primary motor cortex (M1) and post-MF (MEF-I) [8] which is related to the reafferent sensory feedback processing in the primary somatosensory cortex (S1), respectively. Based on its latency, the iN+20 obtained in our experiment (Fig. 1(b)) may reflect the reafferent sensory feedback processing in the right somatosensory cortex (ipsi-lateral to the right finger tapping). These are the interpretations of the peaks in the MEG waveforms during the periodic right-index finger tapping. We confirmed the same interpretation of the MEG waveforms during the left-index finger tapping. In this case, the peaks are observed with inverse polarity due to the spatial direction of the orthogonal tangential derivatives of the magnetic field in the Neuromag 122 system.

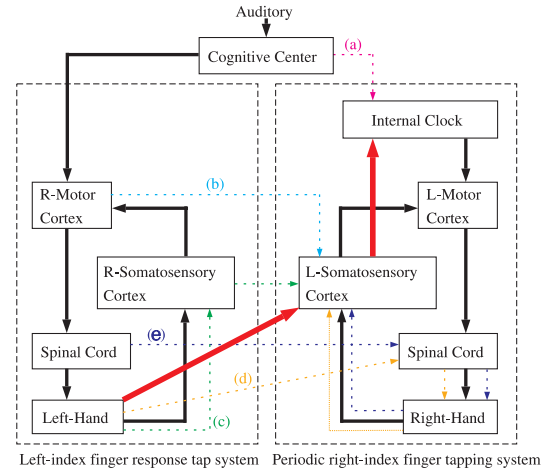


Figure 4: Block diagram of the neural system which controls the periodic right-index finger tapping (right-hand side) and the left-index finger tap (left-hand side). See text for arrows.

Next we discuss the results of the phase resetting experiment. The critical differences between Type 0 and Type 1 reset subjects in the MEG response during the transient period were summarized in the items (i)-(iv) in Sect. 3. Figure 4 shows a block diagram illustrating the periodic right-index finger tapping control system on the right hand side, left-index finger tap system on the left hand side, and the interactions between them. For the periodic right-finger tapping control system, the internal clock

produces a periodic rhythm and drives the left motor cortex periodically. The signal produced at the motor cortex (corresponding to MF in the MEG waveforms) is transmitted to the spinal cord via corticospinal tract leading to discharges of the alpha motoneurons, and finally contractions of the innervated muscles which produce the tapping. Sensory informations are transmitted via afferent feedback routes to the contra-lateral left somatosensory cortex, and generate post-MF peak in MEG. These process are indicated by the arrows in the right-hand side of Fig. 4. For the left-index finger tap system, the right motor cortex is activated by the signal transmitted through the auditory receptors, the auditory cortex and the cognitive center (black arrows from the auditory to R-Motor Cortex in Fig. 4). Below this level, the information flow is the same as the corresponding periodic right-index finger tapping system.

Now based on items (i)-(iv) in Sect. 3, we discuss the neural pathway by which the left-finger tap system affects the periodic right-finger tapping system and results in the phase reset. We propose that the internal clock rhythm is reset by the signals transmitted along the pathway indicated by the thick solid (and red) arrows in Fig. 4. The other pathways indicated by labels (a)-(e) and dotted (and colored) arrows in Fig. 4 can be excluded from candidates for the effective pathways for the phase reset by the following reasons: **(a)** From the (auditory) cognitive center to the interval clock indicated by (a) and the pink arrow in Fig. 4. Reason: In the supplemental experiment, we applied two different signals (i.e., 2000 Hz and 500 Hz tone) to the subjects executing periodic right-finger tapping. The subjects were instructed to respond to the 2000 Hz tone (go-signal) by their left-finger tap as in our main experiment and not to respond to 500 Hz tone (nogo-signal). The subject who showed Type 0 reset in the main experiment showed Type 1 reset to the nogo-signal. **(b)** From the right motor cortex to the left somatosensory cortex indicated by (b) and the light blue arrow. Reason: From item (ii), the right motor cortex was activated at least 80 ms earlier than the left somatosensory cortex. It may be natural to consider that it does not take such a long time from the right motor cortex to the left somatosensory cortex. **(c)** From the left-hand to the left somatosensory cortex via contra-lateral right somatosensory cortex indicated by (c) and the green arrows. Reason: From item (iii), the left somatosensory cortex was activated earlier than the right somatosensory cortex in four out of six subjects. **(d)** Spinal reflex pathway from the left-

hand to the right-hand via spinal cord indicated by (d) and the orange arrows. Reason: From item (iv), the left somatosensory cortex was activated earlier than the first right-index finger tap after the left-index finger tap perturbation for every subjects. The pathways indicated by (e) and the dark blue arrows can be rejected by the same reason as in (d).

In summary, we propose that the tapping rhythm is reset by the following procedure: (1) The afferent feedback signal from the left-hand reaches the ipsi-lateral left somatosensory cortex. (2) The left somatosensory cortex in Type 0 subjects generates larger response to the afferent signal in comparison with Type 1 subjects. (3) This larger response in Type 0 subjects acts as a larger perturbation to the internal clock and to the left motor cortex leading to Type 0 phase reset of the internal clock. (4) Finally, through the efferent corticospinal pathway, the right-index finger tapping rhythm shows Type 0 reset.

References

1. M.A. Pastor and J. Artieda, *Time, Internal Clocks and Movement*, (Elsevier, Amsterdam, 1996).
2. A.T. Winfree, *The Geometry of Biological Time*, (Springer-Verlag, New York, 1980).
3. K. Yoshino, T. Nomura, K. Pakdaman, and S. Sato, "Synthetic analysis of periodically stimulated excitable and oscillatory membrane models", *Phys Rev E* **59**, 956-969, 1999.
4. M.E. Brandt, B.H. Jansen, and N.F. Kharas, "Visual-evoked phase angle resetting of the alpha EEG", In: *Nonlinear dynamical analysis of the EEG*, B.H. Jansen and M.E. Brandt, eds. (World Scientific, Singapore 1993), pp 285-309.
5. D.S. Wagener, and J.G. Colebatch, "Voluntary rhythmic movement is reset by stimulating the motor cortex", *Exp Brain Res* **111**, 113-120, 1996.
6. J. Yamanishi, M. Kawato and R. Suzuki, "Studies on human finger tapping neural networks by phase transition curves", *Biol Cybern* **33**, 199-208, 1979.
7. C. Gerloff, N. Uenishi, T. Nagamine, T. Kunieda, M. Hallett, and H. Shibasaki, "Cortical activation during fast repetitive finger movements in humans: steady state movement-related magnetic fields and their cortical generators", *Electroenceph clin Neurophysiol* **109**, 444-453, 1998.
8. D. Cheyne and H. Weinberg, "Neuromagnetic fields accompanying unilateral finger movements: pre-movement and movement-evoked fields", *Exp Brain Res* **78**, 604-612, 1989.